

## **REMARKS/ARGUMENTS**

Claims 1-6 and 10-14 are currently pending in the above-captioned application.

The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

### **1. Amended Claims.**

Claim 1 has been amended to address the 35 USC §112 objection – see (4) below.

Claim 1 has also been amended to encompass compounds/dyes specifically having 3 to 5 sulfonic acid group substituents. Basis can be found in the specification at page 11 lines 4 to 6. Hence, Applicants contend that no new subject matter has been added by the amendment. The description at page 4 line 28 to page 5 line 11 makes it clear that the term ‘sulfonic acid group’ encompasses  $-\text{SO}_3\text{H}$  and  $-(\text{CH}_2)_k\text{-W}$ , where W is sulfonic acid plus ionized versions thereof, i.e. sulfonate groups.

### **2. Claim Rejections 35 USC §102.**

Claim 1 and dependent claims stand rejected as lacking novelty over the prior art of record. Per the current Office Action, the Examiner’s definition of F includes “alkyl groups substituted with sulfonic acid groups.....”, and that the F affinity tag is defined as a sulfoalkyl group.

Applicants disagree with that analysis. The Examiner refers to page 3 lines 4 to 7 of Applicants previous response (05 March 2009). That text states:

“...when any of groups  $\text{R}^1$  and  $\text{R}^2$  is not said group  $-\text{E}-\text{F}$ , said remaining groups  $\text{R}^1$  and  $\text{R}^2$  are independently selected from  $\text{C}_1-\text{C}_6$  alkyl, benzyl either unsubstituted or

substituted with sulphonic acid, and the group  $-(CH_2)_k-W$ , where W and k are hereinbefore defined”

Applicants point out that the text referred to clearly relates to the definition of groups  $R^1$  and  $R^2$  (not F). It states that when  $R^1/R^2$  is not the group -E-F [emphasis added], it can be various things including sulfoalkyl. Applicants stress that definition is still limited to  $R^1/R^2$  and not -E-F. The group F is defined at (i) (ii) (iii) of present claim 1, and those definitions exclude sulfoalkyl. Applicants therefore maintain their previous position on this matter that claim 1 is novel over the prior art of record.

The Examiner also asserts that the “F affinity tag is defined as a sulfoalkyl group”. No page citation or further explanation was given. Applicants disagree with this analysis also. Thus, the present specification describes what is meant by the term “affinity tag” at two locations - page 10 lines 8 to 21, and page 15 lines 10 to 12. The definition therein is believed clear, and ‘sulfoalkyl’ is outside the scope of the term “affinity tag”. The novelty objections based on the definition of F should therefore be withdrawn.

### **3. Claim Rejections: 35 USC §103.**

Claim 1 and dependent claims stand rejected as being obvious over Leung (US 6,974,873). Applicants respectfully find it problematic that the Examiner apparently believes that everything within the scope of Leung is relevant to obviousness. Teaching by Leung of preferred embodiments which point in a direction outside the scope of the present claims is not regarded as teaching away from modification at other positions, i.e. indolium ring..

Applicants first of all point out that the compounds encompassed by the formula of Leung at Column 3 lines 24 to 34 are vast in scope. With reference to A (Formula I) and B (Formula VII) therein, X and Z are defined to be:



where X and Z are the same or different (Leung Column 4 lines 16 to 23 plus Column 6 lines 4 to 16). Since X and Z can be the same or different, there are 25 combinations of classes of dye. Only one of those corresponds to present claim 1 (X = -CR<sup>3</sup>R<sup>4</sup>- and Z = -CR<sup>13</sup>R<sup>14</sup>-).

A further important difference is that revised claim 1 stipulates at proviso (c), that the compound/dye must have 3 to 5 sulfonic acid substituents. Leung does not disclose, teach or suggest that feature. Leung teaches that sulfonation of the dyes is an optional feature. Only at Column 10 lines 53 to 54 does Leung suggest that, in one aspect, the dyes “are sulfonated one or more times”. Leung mentions (Column 10 line 64 following) in the context of attaching the reactive group at R<sup>3</sup> only, sulfonation at least 4 times. That is specifically at R<sup>7</sup>, R<sup>17</sup> and sulfoalkyl at R<sup>2</sup> and R<sup>13</sup>. That combination is outside the scope of the present claims.

A further essential feature of present claim 1 is that one group -E-F is attached – no more, no less. Leung does not disclose, teach or suggest that feature. In contrast, Leung makes that feature optional. Hence, there could be zero such groups in Leung. There could

also be a large number of them - since such a group is an optional definition for almost all the R groups of Leung. Leung does teach (Column 12 lines 1 to 11) that, “in one embodiment” at least one such group should be present. That is, however, merely one of many preferred embodiments of Leung and the general teaching therein is very much broader as described above.

A further feature of present claim 1 is that at least one of  $R^{11}$  to  $R^{14}$  of Formula I is required to be  $-(CH_2)_k-W$  and the remainder are required to be  $C_{1-6}$  alkyl. See proviso (b) of amended claim 1. Leung does not disclose, teach or suggest that combination of features. Instead, the  $R^3/R^4/R^{13}/R^{14}$  groups of Leung are freely chosen from a long list of possibilities.

Present Formula I also specifies the combination that, when  $R^1/R^2$  is not  $-E-F$ , it is chosen from  $C_{1-6}$  alkyl,  $-(CH_2)_k-W$  or benzyl (optionally substituted with sulfonic acid). Leung does not disclose, teach or suggest that combination. The corresponding groups of Leung ( $R^2$  and  $R^{12}$ ) are independently chosen from a long list of possibilities (Leung Columns 4 lines 24 to 54). Leung in fact teaches that it is preferred that  $R^2$  and  $R^{12}$  are the same (Column 4 lines 54-55).

The present invention also teaches that the group  $-E-F$  can be located at the  $R^7$  groups of Formula I. Leung does not disclose, teach or suggest that feature. Thus, Leung describes the BRIDGE at Column 6 line 47 ff (Formula VIII therein). The definitions of  $R^{21-27}$  (*ibid*, Column 6 line 66 to Column 7 line 16), in Leung exclude that possibility.

The compounds of Formula I of present claim 1 are thus believed to have several features and/or combinations of features not disclosed, taught or suggested by Leung. These features make the invention much more than mere “positional isomers of Leung’s compound” as suggested by the Examiner.

The Examiner also alleges that “the structural backbone of the cyanine molecule” are the same. Applicants point out that the basic skeleton of cyanine dyes has indeed been known for some decades. That has not, however, prevented patenting in the area and many hundreds of patents have been granted on cyanine dye type molecules. See eg. Leung at Column 1 lines 16 to 48, plus Column 2 lines 19 to 28 for an illustration of patent activity in the field. The person skilled in the art would know that dye chemistry is such that small changes in both substituent pattern and choice of substituents can have profound effects on the properties of a given dye for a particular application. Leung itself provides an illustration of the subtle effects of substituents – see Column 1 line 49 to Column 2 line 16 of Leung. The dyes of present amended claim 1 have useful improved properties – see page 11 lines 4 to 14 of the specification.

In view of all the above, Applicants contend that the obviousness rejection based on Leung should be withdrawn.

**4. Claim Rejection: 35 USC §112.**

Claims 1, 2-6, and 10-14 stand rejected in this regard.

The phraseology “remaining groups” is used throughout claim 1. As stated therein, one of groups  $R^{1-7}$  is -E-F and the “remaining groups” (i.e. those which are not -E-F) are defined.

Claim 1 has been amended to define the various numbered R groups more positively, and to include the definition -E-F explicitly within the scope for each. The requirement that one -E-F group is present is made new proviso (a).

Similar logic applies to groups  $R^{11-14}$ , where at least one is  $-(CH_2)_k-W$  and the “remaining groups” are defined. This has been recast within the definition of  $R^{11-14}$ , together with new proviso (b).

Claim 1 has also been amended to present the definition of the  $R^{1-14}$  groups in numeral order.

The scope of amended claim 1 is now believed clear. Clarifying amendments have been made to claims 2 and 3 also to delete redundant language.

The 35 USC §112 objections are therefore believed to have been overcome.

### **CONCLUSION**

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims, 1-6 and 10-14 are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

/Craig Bohlken/  
Craig Bohlken  
Reg. No. 52,628  
Attorney for Applicants

GE Healthcare, Inc.  
101 Carnegie Center  
Princeton, NJ 08540  
Tel: (609) 514-6530  
Fax: (609) 514-6572